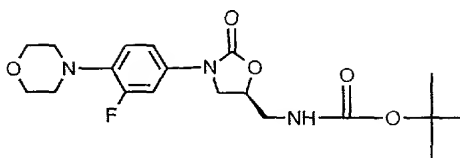


EXAMPLE 6

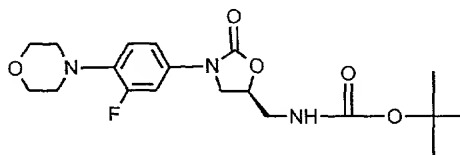


5 Preparation of tert-butyl {(5S)-3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methylcarbamate (Compound III, R¹ = 3-fluoro-4-(4-morpholinyl)phenyl, R³=t-butyl)

To a solution of [3-fluoro-4-(4-morpholinyl)phenyl]carbamic acid
10 phenylmethyl ester (Example 1) (0.8758 g, 2.651 mmol) and tert-butyl (2S)-chloro-2-hydroxypropylcarbamate (Example 3) (0.7011 g, 3.344 mmol, 1.26 eq) in DMF (1.7 ml) in an ice bath was added a solution of lithium t-butoxide in THF (2.82 g of an 18.1 wt% solution, 6.37 mmol, 2.40 eq). The resultant solution was allowed to stand at 20°C for 44 hours (HPLC showed 95.0% conversion after 20 hours and 97.8%
15 conversion after 44 hours). Saturated aqueous ammonium chloride (5.0 ml), water (10 ml) and methylene chloride (12 ml) were added and the phases separated. The aqueous layer was washed with methylene chloride (12 ml) and the combined organics dried on magnesium sulfate and concentrated to an oil (2.4574 g). External standard HPLC showed the oil to contain 0.9397 g (89.6%) of Compound III, wherein
20 R¹ = 3-fluoro-4-(4-morpholinyl)phenyl, R³=t-butyl. HPLC retention time = 4.97 min (column = Zorbax SB-C8 3.5 micron 150 X 4.6 mm, flow rate = 2.0 ml/min, gradient elution from 30:70 A:B to 90:10 A:B over 15 minutes; A = 969:30:1 acetonitrile: THF: trifluoroacetic acid; B= 949:50:1 water: THF: trifluoroacetic acid). An analytical sample of Compound III, R¹ = 3-fluoro-4-(4-morpholinyl)phenyl, R³=t-butyl isolated by column chromatography (ethyl acetate/ hexanes eluent) had the
25 following physical properties: mp 46.2-48.0°C; ¹H-NMR (CDCl₃, 400 MHz) δ: 7.43 (dd, J = 14.4, 2.4 Hz, 1H) 7.09 (dd, J = 8.8, 2.0 Hz), 6.92 (t, J = 9.2, 1H) 5.11 (bs, 1H), 4.73 (bs, 1H), 4.00 (t, J = 8.8, 1H), 3.86 (t, J = 4.4, 4H), 3.80 (t, J = 6.8, 1H), 3.50 (m, 2H), 3.04 (t, J = 4.8, 4H), 1.41 (s, 9H); ¹³C-NMR (CDCl₃, 100 MHz) d 28.25

(q), 43.27 (t), 47.53 (t), 51.03 (dt, $J_{C-F} = 3.02$ Hz), 66.95 (t), 71.99 (D), 80.19 (s),
107.50 (dd, $J_{C-F} = 26.16$ Hz), 113.93 (dd, $J_{C-F} = 3.02$ Hz), 118.83 (dd, $J_{C-F} = 4.03$ Hz),
133.18 (sd, $J_{C-F} = 11.07$ Hz), 136.45 (sd, $J_{C-F} = 9.06$ Hz), 154.29 (s), 155.55 (sd, $J_{C-F} =$
241.50 Hz), 156.30 (s). MS (EI) m/z (relative intensity) 395 (100), 339 (85); $[\alpha]^{25}_D -$
5 36 (C 0.71, acetonitrile); Anal Calcd for $C_{19}H_{26}FN_3O_5$: C, 57.71; H, 6.63; N, 10.63;
found: C, 57.63; H, 6.81; N, 10.32.

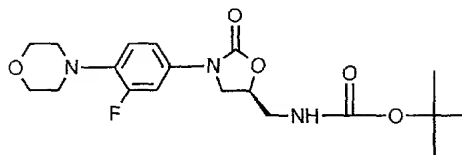
EXAMPLE 7



10
15 **Alternative preparation of tert-butyl {(5S)-3-[3-fluoro-4(4-morpholinyl)phenyl]-2-oxo-1,3-oxazolidin-5-yl} methylcarbamate (Compound III, $R^1 = 3$ -fluoro-4-(4-morpholinyl)phenyl, $R^3 = t$ -butyl).**

To a slurry of [3-fluoro-4(4-morpholinyl)phenyl]carbamic acid
phenylmethyl ester (Example 1) (1.0039 g, 3.039 mmol) and tert-butyl
(2S)oxiranylmethylcarbamate (Example 5) (0.653 g, 3.77 mmol, 1.24 eq) in THF (1.5
20 ml) at 0°C was added a solution of lithium t-butoxide in THF (18.07 wt%, 1.735 g,
3.92 mmol, 1.29 eq). After standing 2 days at 20-25° C, methylene chloride (5.0 ml),
then acetic acid (0.35 ml, 6.11 mmol, 2.01 eq) followed by water (3.5 ml) was added.
The phases were separated and the aqueous washed with methylene chloride (3.5 ml).
The combined organics were dried on magnesium sulfate and concentrated to an oil
25 which was shown to contain 1.03 g (85.7%) of Compound III, wherein $R^1 = 3$ -fluoro-
4-(4-morpholinyl)phenyl, $R^3 = t$ -butyl, by external standard HPLC: retention time =
4.06 min (column = Zorbax SB-C8 3.5 micron 150 X 4.6 mm, flow rate = 2.0 ml/min,
gradient elution from 30:70 A:B to 90:10 A:B over 15 minutes; A = 969:30:1
acetonitrile: THF: trifluoroacetic acid; B = 949:50:1 water: THF:trifluoroacetic acid).

EXAMPLE 8



- 5 **Alternative preparation of tert-butyl {(5S)-3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methylcarbamate (Compound III, R¹ = 3-fluoro-4-(4-morpholinyl)phenyl, R³=t-butyl)**

To a solution of [3-fluoro-4-(4-morpholinyl)phenyl]carbamic acid
10 phenylmethyl ester, (Example 1) (0.1646 g, 0.498 mmol) and (1S)-2-[(tert-butoxycarbonyl)amino]-1-(chloromethyl) ethyl acetate, (Example 4) (0.1534 g, 0.609 mmol, 1.22 eq) in DMF (0.344 g) and methanol (0.0195 g, 0.609 mmol, 1.22 eq) at 0°C was added lithium t-butoxide (0.0881 g, 1.101 mmol, 2.21 eq). The solution was allowed to stand at 20-25°C for 18 h. Acetic acid (0.057 ml, 0.996 mmol, 2.00 eq)
15 was added. The mixture was diluted to 250 ml total volume with methanol. The resultant solution was shown to contain 0.186 g (94.6%) of Compound III, wherein R¹ = 3-fluoro-4-(4-morpholinyl)phenyl, R³=t-butyl by external standard HPLC: retention time = 4.10 min (column = Zorbax SB-C8 3.5 micron 150 X 4.6 mm, flow rate = 2.0 ml/min., gradient elution from 30:70 A:B to 90:10 A:B over 15 minutes; A = 969:30:1
20 acetonitrile: THF: trifluoroacetic acid; B = 949:50:1 water: THF: trifluoroacetic acid).

EXAMPLE 9

